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PTO/SB/21 (09-06)
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# TRANSMITTAL FORM

*(to be used for all correspondence after initial filing)*

| | |
|---|---|
| Total Number of Pages in This Submission | 17 |

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| Application Number | 10/577,907 |
| Filing Date | May 1, 2006 |
| First Named Inventor | Graham MCINTYRE |
| Art Unit | Unknown |
| Examiner Name | Unknown |
| Attorney Docket Number | 15131.0003 |

## ENCLOSURES *(Check all that apply)*

- ☐ Fee Transmittal Form
  - ☐ Fee Attached
- ☐ Amendment/Reply
  - ☐ After Final
  - ☐ Affidavits/declaration(s)
- ☐ Extension of Time Request
- ☐ Express Abandonment Request
- ☐ Information Disclosure Statement
- ☐ Certified Copy of Priority Document(s)
- ☐ Reply to Missing Parts/ Incomplete Application
  - ☐ Reply to Missing Parts under 37 CFR 1.52 or 1.53
- ☐ Drawing(s)
- ☐ Licensing-related Papers
- ☐ Petition
- ☐ Petition to Convert to a Provisional Application
- ☐ Power of Attorney, Revocation Change of Correspondence Address
- ☐ Terminal Disclaimer
- ☐ Request for Refund
- ☐ CD, Number of CD(s) _____
  - ☐ Landscape Table on CD
- ☐ After Allowance Communication to TC
- ☐ Appeal Communication to Board of Appeals and Interferences
- ☐ Appeal Communication to TC **(Appeal Notice, Brief, Reply Brief)**
- ☐ Proprietary Information
- ☐ Status Letter
- ☑ Other Enclosure(s) (please Identify below):
  International Preliminary Report on Patentability (16 pgs)

Remarks

## SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

| | | | |
|---|---|---|---|
| Firm Name | STEPTOE & JOHNSON LLP | | |
| Signature | | | |
| Printed name | Harold H. Fox | | |
| Date | October 30, 2006 | Reg. No. | 41,498 |

## CERTIFICATE OF TRANSMISSION/MAILING

I hereby certify that this correspondence is being facsimile transmitted to the USPTO or deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on the date shown below:

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| Typed or printed name | | Date | |

# PATENT COOPERATION TREATY

From the INTERNATIONAL BUREAU

# PCT

NOTIFICATION CONCERNING TRANSMITTAL OF COPY OF INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY (CHAPTER I OF THE PATENT COOPERATION TREATY)
(PCT Rule 44bis.1(c))

To:

WILLIAMS, Aylsa
D. Young & Co.
120 Holborn
London EC1N 2DY
ROYAUME UNI



| | |
|---|---|
| Date of mailing *(day/month/year)*<br>26 May 2006 (26.05.2006) | |
| Applicant's or agent's file reference<br>P17854WO AAW | **IMPORTANT NOTICE** |

| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/GB2004/004783 | 12 November 2004 (12.11.2004) | 14 November 2003 (14.11.2003) |

Applicant
UCL BIOMEDICA PLC et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

| | |
|---|---|
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland | Authorized officer<br>Nora Lindner |
| Facsimile No.+41 22 740 14 35 | Facsimile No.+41 22 338 89 65 |

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

| | | |
|---|---|---|
| Applicant's or agent's file reference<br>P17854WO AAW | **FOR FURTHER ACTION** | See item 4 below |
| International application No.<br>PCT/GB2004/004783 | International filing date *(day/month/year)*<br>12 November 2004 (12.11.2004) | Priority date *(day/month/year)*<br>14 November 2003 (14.11.2003) |
| International Patent Classification (8th edition unless older edition indicated)<br>See relevant information in Form PCT/ISA/237 | | |
| Applicant<br>UCL BIOMEDICA PLC | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 15 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

| | | |
|---|---|---|
| ☒ | Box No. I | Basis of the report |
| ☒ | Box No. II | Priority |
| ☒ | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| ☒ | Box No. IV | Lack of unity of invention |
| ☒ | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| ☒ | Box No. VI | Certain documents cited |
| ☐ | Box No. VII | Certain defects in the international application |
| ☒ | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

| | |
|---|---|
| | Date of issuance of this report<br>15 May 2006 (15.05.2006) |
| The International Bureau of WIPO<br>34, chemin des Colombettes<br>1211 Geneva 20, Switzerland<br><br>Facsimile No. +41 22 740 14 35 | Authorized officer<br>Nora Lindner<br><br>Telephone No. +41 22 338 89 65 |

Form PCT/IB/373 (January 2004)

# PATENT COOPERATION TREATY



From the
INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

| | |
|---|---|
| Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet) | |
| Applicant's or agent's file reference<br>see form PCT/ISA/220 | **FOR FURTHER ACTION**<br>See paragraph 2 below |
| International application No.<br>PCT/GB2004/004783 | International filing date *(day/month/year)*<br>12.11.2004 |
| Priority date *(day/month/year)*<br>14.11.2003 | |
| International Patent Classification (IPC) or both national classification and IPC<br>A61K39/39, A61P9/00, A61P37/00, A61P37/06 | |
| Applicant<br>UCL BIOMEDICA PLC | |

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office - P.B. 5818 Patentlaan 2
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Authorized Officer

Noë, V

Telephone No. +31 70 340-4181

**WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/GB2004/004783

**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**Box No. II Priority**

1. ☐ The following document has not been furnished:

   ☐ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. ☒ The International Searching Authority has not been able to consider the validity of the priority claim because a copy of the earlier application whose priority has been claimed was not available to the International Searching Authority at the time that the search was conducted (Rule 17.1). This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

4. Additional observations, if necessary:

**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 24-25(completely), 1-23(partially)

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the whole application or for said claims Nos. 24-25 (completely), 1-23 (partially)

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

| | | |
|---|---|---|
| the written form | ☐ | has not been furnished |
| | ☐ | does not comply with the standard |
| the computer readable form | ☐ | has not been furnished |
| | ☐ | does not comply with the standard |

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

## Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

   ☒ paid additional fees.

   ☐ paid additional fees under protest.

   ☐ not paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

   ☐ complied with

   ☒ not complied with for the following reasons:

   **see separate sheet**

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☐ all parts.

   ☒ the parts relating to claims Nos. 1-23 (partially)

## Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | 8-10,20-22 |
| | No: | Claims | 1-7,11-19,23 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-23 |
| Industrial applicability (IA) | Yes: | Claims | 1-11 |
| | No: | Claims | |

2. Citations and explanations

   **see separate sheet**

## Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

   and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

   **see form 210**

## Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

## IV. Lack of unity (Continuation)

The present application does not satisfy the requirements of Rule 13.1,13.2 and 13.3 PCT as the requisite unity of invention does not exist inasmuch as a technical relationship involving one or more of the same or corresponding special technical features does not exist between the subject-matter of the following inventions.
The technical problem underlying the present application is the provision of immune modulator compositions for the treatment or prevention of autoimmune diseases or disorders comprising a whole cell of a bacterium from the order Actinomycetales.

The solutions to this technical problem provided by the application are :

1) claims 1-23 (partially) : use of an immune modulator composition comprising a whole cell bacterium from the genus Rhodococcus for the treatment or prevention of autoimmune diseases or disorders

2) claims 1-23 (partially) : use of an immune modulator composition comprising a whole cell bacterium from the genus Gordonia for the treatment or prevention of autoimmune diseases or disorders

3) claims 1-23 (partially) : use of an immune modulator composition comprising a whole cell bacterium from the genus Nocardia for the treatment or prevention of autoimmune diseases or disorders

4) claims 1-23 (partially) : use of an immune modulator composition comprising a whole cell bacterium from the genus Dietzia for the treatment or prevention of autoimmune diseases or disorders

5) claims 1-23 (partially) : use of an immune modulator composition comprising a whole cell bacterium from the genus Tsukamurella for the treatment or prevention of autoimmune diseases or disorders

6) claims 1-23 (partially) : use of an immune modulator composition comprising a whole cell bacterium from the genus Nocardioides for the treatment or prevention of autoimmune diseases or disorders

Different prior art documents disclose immune modulator compositions for the treatment or prevention of autoimmune diseases or disorders comprising a whole cell of a bacterium from the order Actinomycetales.

WO03049752 : discloses the use of a bacterial preparation comprising killed Rhodococcus or Nocardia bacteria for the treatment of autoimmune disease e.g. rheumatoid arthritis (see page 4, line 22-27; page 6, line 5-8; claims 3,5,15 and 16).

AU706122 : discloses the use of killed Mycobacterium vaccae bacteria, belonging to the order Actinomycetales, for the treatment of vascular diseases which are immunologically mediated (see page 4, line 3-22; example 2 and 4; claims 1-3 and 9-11).

Conforti et al., European Journal of Pharmacology (1997): 324, 241-247 : discloses that the treatment with Mycobacterium Butyricum, belonging to the order Actinomycetales, suppresses adjuvant induced arthritis (see abstract).

WO8505034 : discloses the use of whole cell Mycobacterium vaccae for the prevention and treatment of arthritic diseases (see abstract; page 2, line 3-9 and 15-22; page 5, line 25 - page 6, line 7; claims 1,6,10).

In view of these prior art documents, the technical problem can be defined as the provision of alternative immune modulator compositions for the treatment or prevention of autoimmune diseases or disorders comprising a whole cell of a bacterium from the order Actinomycetales. Taking into account the disclosure in the prior art, bearing in mind the essential differences among the solutions provided (see above 1-6) and considering that no other technical feature can be acknowledged which in the light of the prior art, could be regarded as a special technical feature in the sense of Rule 13.2 PCT, the International

Search Authority is of the opinion that there is no single inventive concept underlying the plurality of inventions of the present application in the sense of Rule 13.1 PCT. Consequently there is lack of unity and the different invention not belonging to a common inventive concept are formulated as the different subjects in the communication pursuant to Article 17(3)(a) PCT.
In response to the invitation to pay additional fees, the applicant paid two fees to cover search and examination of inventions 2 and 5.

## V. **Reasoned statement** (Continuation)

1 CITATIONS

Reference is made to the following documents:

D1: WO 03/049752 A (INSTITUT PASTEUR; INSTITUT NATIONAL DE LA SANTE ET DE LA RECHERCHE MED) 19 June 2003 (2003-06-19)

D2: WO 2004/022093 A (UNIVERSITY COLLEGE LONDON; MCINTYRE, GRAHAM; STANFORD, JOHN, LAWSON; S) 18 March 2004 (2004-03-18)

2 NOVELTY (Art. 33(2) PCT)

2.1 **Invention 1** : use of an immune modulator composition comprising a whole cell bacterium from the genus **Rhodococcus** for the treatment or prevention of autoimmune diseases or disorders

2.1.1 D1 discloses the use of a bacterial preparation comprising killed Rhodococcus bacteria for the treatment of autoimmune disease e.g. rheumatoid arthritis (see page 4, line 22-27; page 6, line 5-8; claims 3,5,15 and 16). In view of D1, the subject-matter of claims 1-7,11-19,23 is not novel.

2.1.2 The present application does not satisfy the criterion set forth in Article 33(2) PCT because the subject-matter of claims 1-7,11-19,23 is not new in respect of

prior art as defined in the regulations (Rule 64(1)-(3) PCT).

2.2 **Invention 2** : use of an immune modulator composition comprising a whole cell bacterium from the genus **Gordonia** for the treatment or prevention of autoimmune diseases or disorders

2.2.1 In view of the prior art cited, the subject-matter of claims 1-23 is considered to be novel and satisfies the criterion set forth in Article 33(2).

2.3 **Invention 5** : use of an immune modulator composition comprising a whole cell bacterium from the genus **Tsukamurella** for the treatment or prevention of autoimmune diseases or disorders

2.3.1 In view of the prior art cited, the subject-matter of claims 1-23 is considered to be novel and satisfies the criterion set forth in Article 33(2)

3 INVENTIVE STEP (Art. 33(3) PCT)

3.1 **Invention 1** : use of an immune modulator composition comprising a whole cell bacterium from the genus **Rhodococcus** for the treatment or prevention of autoimmune diseases or disorders.

3.1.1 Dependent claims 8-9 and 20-21 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step because it would be obvious for the skilled person, to use an immunomodulatory composition which is known for the treatment of autoimmune diseases also for the treatment of chronic graft rejection.

3.1.2 Dependent claims 10 and 22 do not appear to contain any additional features which, in combination with the features of any claim to which they refer, involve an inventive step because the use of the specific Rhodococcus bacteria is merely a straightforward possibility from which the skilled person would select without the exercise of inventive skills.

3.1.3 The present application does therefore not satisfy the criterion set forth in Article 33(3) PCT and the subject-matter of claims 8-110 and 20-22 does not involve an inventive step (Rule 65(1)(2) PCT).

3.2 **Invention 2** : use of an immune modulator composition comprising a whole cell bacterium from the genus **Gordonia** for the treatment or prevention of autoimmune diseases or disorders

3.2.1 For inventive step analysis of claim 1, document D1 is considered to represent the closest prior art and discloses the use of a bacterial preparation comprising killed Actinomycetes bacteria comprising Mycobacteria, Nocordia and Rhodococcus for the treatment of autoimmune disease e.g. rheumatoid arthritis (see page 4, line 22-27; page 6, line 5-8; claims 3,5,15 and 16). The subject-matter of claim 1 differs in that the use of use of an immune modulator composition comprising a whole cell bacterium from the genus **Gordonia** for the treatment or prevention of autoimmune diseases or disorders is claimed.

3.2.2 The problem to be solved by the subject matter of claim 1 may therefore be regarded as the provision of an alternative immune modulator composition for the treatment or prevention of autoimmune diseases or disorders. The solution would be the provision of an immune modulator composition comprising a whole cell bacterium from the genus **Gordonia** for the treatment or prevention of autoimmune diseases or disorders.

3.2.3 This solution is considered to involve an inventive step because none of the

prior art documents suggests the use of bacteria from the genus Gordonia as an immune modulator for the treatment or prevention of autoimmune diseases or disorders and this would not be obvious for the skilled person. Therefore, the subject-matter of claim 1 and dependent claims 2-11 is considered to be inventive.

3.2.4 Claims 12-23 related to methods of treatment using the composition of claim 1, are for the same reasons also considered to be inventive.

3.3 **Invention 5** : use of an immune modulator composition comprising a whole cell bacterium from the genus **Tsukamurella** for the treatment or prevention of autoimmune diseases or disorders

3.3.1 For inventive step analysis of claim 1, document D1 is considered to represent the closest prior art and discloses the use of a bacterial preparation comprising killed Actinomycetes bacteria comprising Mycobacteria, Nocordia and Rhodococcus for the treatment of autoimmune disease e.g. rheumatoid arthritis (see page 4, line 22-27; page 6, line 5-8; claims 3,5,15 and 16). The subject-matter of claim 1 differs in that the use of use of an immune modulator composition comprising a whole cell bacterium from the genus **Tsukamurella** for the treatment or prevention of autoimmune diseases or disorders is claimed.

3.3.2 The problem to be solved by the subject matter of claim 1 may therefore be regarded as the provision of an alternative immune modulator composition for the treatment or prevention of autoimmune diseases or disorders. The solution would be the provision of an immune modulator composition comprising a whole cell bacterium from the genus **Tsukamurella** for the treatment or prevention of autoimmune diseases or disorders.

3.3.3 This solution is considered to involve an inventive step because none of the

prior art documents suggests the use of bacteria from the genus **Tsukamurella** as an immune modulator for the treatment or prevention of autoimmune diseases or disorders and this would not be obvious for the skilled person. Therefore, the subject-matter of claim 1 and dependent claims 2-11 is considered to be inventive.

3.3.4 Claims 12-23 related to methods of treatment using the composition of claim 1, are for the same reasons also considered to be inventive.

4 INDUSTRIAL APPLICABILITY (Art. 33(4) PCT)

4.1 For the assessment of the present claims 12-23 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

## VI. Certain documents cited (Continuation)

5.1 Certain published documents

| Application No Patent No | Publication date *(day/month/year)* | Filing date *(day/month/year)* | Priority date *(valid claim)* *(day/month/year)* |
|---|---|---|---|
| WO 2004/022093 | 18/03/2004 | 05/09/2003 | 06/09/2002<br>22/07/2003 |

5.2 The priority documents pertaining to the present application were not available at the time of establishing this first written opinion. Hence, it is based on the assumption

that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct, the above document cited in the international search report could become relevant to assess whether the claimed subject matter satisfy the criteria set forth in Art. 33(1) PCT.

## VIII. Certain observations on the international application (Continuation)

6.1 Claims 7 and 19 have features between brackets which result in a lack of clarity (Art. 6 PCT).